

Agent's file reference: P887 PC00
International application No. PCT/DK03/00448
Applicant: Aarhus Universitet et al.

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Amended Claims

1. A method for estimating the skin cancer, lung cancer, breast cancer and colon cancer risk of an individual comprising

- assessing in the genetic material of a sample from said individual a sequence polymorphism

- in a region corresponding to SEQ ID NO: 2, or a part thereof, or
- in a region complementary to SEQ ID NO: 2, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 2, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 2, or a part thereof,
- obtaining a sequence polymorphism response,

- estimating the skin cancer, lung cancer, breast cancer and colon cancer risk of said individual based on the sequence polymorphism response.

2. The method according to claim 1, wherein a sequence polymorphism is assessed

- in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- in a region complementary to SEQ ID NO: 1, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof.

3. The method according to claim 1, wherein the cell sample is a blood sample, a tissue sample, a sample of secretion, semen, ovum, a washing of a body surface, such as a buccal swap, a clipping of a body surface, including hairs and nails.

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4. The method according to any of the preceding claims, wherein the cell is selected from white blood cells and tumor tissue.

5 5. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one mutation base change.

6. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two base changes.

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7. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one single nucleotide polymorphism.

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8. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two single nucleotide polymorphisms.

9. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least one tandem repeat polymorphism.

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10. The method according to any of the preceding claims, wherein the sequence polymorphism comprises at least two tandem repeat polymorphisms.

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11. The method according to any of the preceding claims, wherein the assessment is conducted by means of at least one nucleic acid primer or probe, such as a primer or probe of DNA, RNA or a nucleic acid analogue such as peptide nucleic acid (PNA) or locked nucleic acid (LNA).

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12. The method according to claim 11, wherein the nucleotide primer or probe is capable of hybridising to a subsequence of the region corresponding to SEQ ID NO: 1, or a part thereof, or a region complementary to SEQ ID NO:1.

13. The method according to claim 11, wherein the primer or probe has a length of at least 9 nucleotide or peptide monomers.

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14. The method according to any of the preceding claims 11-13, wherein at least one primer or probe is capable of hybridising to a subsequence selected from the group of subsequences

- 5 1. GCTCTGAAAC TTACTAGCCC(A/G)GTATTTATGG AGAGGCATTT
2. GTGGTCAAAT TCTCATT CAT CGTGG (T/C) CCAGGCAAGC
ACACTTCCTC
3. ACCCTGAGGT GAGCACCTGT TCCTT(C/T) TCCTTGCCCT TAGCCCA-
GAG GTAGA
10 4. GGGCAGGGGT TTGTGCCTCC AATGA (G/A) CACAAGCTCC
CCCTGCCCCC CAACT
5. CCTGGCGGTG GCCGTACCA GCTTT (T/C) GGGGGTGT
GGGAAGCTGG
6. CTCCAGCCCC ACTGTTCCCT (A/G) GGCCCTATTG GTCCCCCTGG
15 7. ACAAGGAGGA GGCAGAAAGTG AGGTT (G/C) AAACCCACTG CCCAATC-
TTA
8. CCAACACGGT GAAACCCCGT CTGTA(T/C)TAAAAATACA AAAATTAGCC
9. AATCCAGGAC CCCATAATCT TCCGT (C/T) ATCTAAAACA ATA-
ATGGTGA
20 10. CCAAGGGGG CGAGGGGAGG GTGAA (A/G)GGGTGGGACG
GGGGCAGCCG
11. GAAGTGAGAA GGGGGCTGGG GGTG (G/-) CGCTCGCTAG
CGGGCGCGGG
12. CGCAGCGCA GTATCCCGAT TGGCT (C/G)TGCCCTAGCG GATT-
25 GACGGG
13. AACTCCTGGG TTCGATCAAT ACTCA (GACA/-) ATCTTGGCAG
GCGCAGGAGG
14. GCTGGGATTA CAGGCTTGAG CCACC (A/G) CGCCCGGCCT
GCAAAGCCAT
30 15. TTTTGTATCT TTAGTAGAGA CAGG (T/G) TTTCTCCATG TTGGTCAGGC
16. GCCTCAGCCT CCCGAGTAGC TGAGACT (C/A) CAGGTGCCCC CCAC-
CACGCC
17. TGAAATTGTA GGTGAGAGG CCAGGCG (C/T) GGTGCTCAGC
CCTGTAATTT
35 18. GTTTATAAAC ATTAACCAG (T/A) GCTGTGTGAA GGCACCTAAT

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19. CCGTCTCTAT TAAAAATATA AAA (A/C) AATTTAGCCG GGTGTAGCGG
20. GGGAGGCTCG AGGCGGGC (A/G) GATTGCATGA GCTCAGGATT
21. TCCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATT
22. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCACT CCAGCCTGGG
5 23. TCTTAGGACG CATGGGGGT (T/G) GAGAGAACGG GGAGATAGAC
24. CTGGGTTCTA GAACTACC (C/T) ATGCAAACCC AGCTGTTTCC
25. ATTCTGCCCT GGGTTCTAGA ACTACCT (C/A) TGCAAACCCA
GCTGTTTCCC
26. GCTGTTTCCC ACCCCATAAG GCA (A/G) TAGGGGAGCC
10 CACCTCCGCC
27. GACCTAGAAG ATCGGTCGAG A (C/T) AGCAGCTTGA GGCTGGCAGG
28. CTGGCCAGGA ATGCAGTCGG GTCAC (C/T) CTGTCTAGCC
ACCGTCTCGC
29. GGGAGGAGTC GCCGATCAGG (C/T) CCCTTCCTGA AAGTCATCGA
15 30. GCAGCCCGGG CTACAGGGTT (A/G) CCTGAGGTGT GGGTCCCAGG
31. TAGAAATACT AACAAAGGGC (T/C) GTGGGTTTCT CCCCCTGCTT
32. ACAGGAGAGG GAAGGTTTTTTG (A/T) TTTTTTTTTT GTTTTTTTTT
33. GAAGAGGAAG AAGCCCAAAG GGA (A/C) AGAAACCTTC GAGCCA-
GAAG
20 34. GCGCCTCAAC AGCCAGAAGG AGCG (A/G) AGCCTCAGGC CCAGG-
CAGCT
35. TTGAGACTCT CTGTTTGAT (A/G) CTTCACTCAG AAGGTGCTTC
36. AGGCCAGGCT CCTGCTGGCT G (C/G) GCTGGTGAG TCTCTGGGGA
37. CCCCTATACC CTCAAGCAT (C/T) TATCCATTGA GTTACAAACA
25 38. ACCATCCCCC GCCTTCCGTT (A/C) GTCCGGCCCC CGAGGCTAGC

or to a sequence complementary to any of the subsequences.

15. The method according to claim 14, wherein at least one nucleotide probe is se-
30 lected from the group consisting of

1. TGAAATTGTA GGTTGAGAGG CCAGGCG (C/T) GGTGCTCAGG
CCTGTAATTT
2. GTTTATAAAG ATTAACCAG (T/A) GCTGTGTGAA GGCACCTAAT
35 3. CCGTCTCTAT TAAAAATATA AAA (A/C) AATTTAGCCG GGTGTAGCGG

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4. GGGAGGCTCG AGGCGGGC (A/G) GATTGCATGA GCTCAGGATT
5. TCCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATTC
6. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCACT CCAGCCTGGG
7. TCTTAGGACG CATGGGGGT (T/G) GAGAGAACGG GGAGATAGAC
5 8. CTGGGTTCTA GAACTACC (C/T) ATGCAAAACC AGCTGTTTCC
9. ATTCTGCCCT GGGTTCTAGA ACTACCT (C/A) TGCAAACCCA
GCTGTTTCCC
10. GCTGTTTCCC ACCCCATAAG GCA (A/G) TAGGGGAGCC
CACCTCCGCC
10 11. GACCTAGAAG ATCGGTGAG A (C/T) AGCAGCTTGA GGCTGGCAGG
12. CTGGCCAGGA ATGCAGTCGG GTCAC (C/T) CTGTCTAGCC
ACCGTCTCGC
13. GGGAGGAGTC GCCGATCAGG (C/T) CCCTTCCTGA AAGTCATCGA
14. GCAGCCCAGG CTACAGGGTT (A/G) CCTGAGGTGT GGGTCCCAGG
15 15. TAGAAATACT AACAAAGGGC (T/C) GTGGGTTTCT CCCCCTGCTT
16. ACAGGAGAGG GAAGGTTTTTTG (A/T) TTTTTTTTTT GTTTTTTTTT
17. GAAGAGGAAG AAGCCCAAAG GGA (A/C) AGAAACCTTC GAGCCA-
GAAG
18. GCGCCTCAAC AGCCAGAAGG AGCG (A/G) AGCCTCAGGC CCAGG-
20 CAGCT

or to a sequence complementary to any of the subsequences.

16. The method according to claim 15, wherein at least one nucleotide probe is se-
25 lected from the group consisting of

1. GTTTATAAAC ATTAAACCAG (T/A) GCTGTGTGAA GGCACTTAAT
2. CCGTCTCTAT TAAAAATATA AAA (A/C) AATTTAGCCG GGTGTAGCGG
3. GGGAGGCTCG AGGCGGGC (A/G) GATTGCATGA GCTCAGGATT
30 4. TCCCAAGTTT CAGGGCCCAA (T/G) ATTCTCAAAT CACAGGATTC
5. TGCAGTGAGC TGAGATCGC (A/G) CCACTGCACT CCAGCCTGGG
or to a sequence complementary to any of the subsequences.

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17. The method according to any of the preceding claims, wherein at least one sequence polymorphism is assessed in a region corresponding to SEQ ID NO: 1 position 1521-37752 (J).

5 18. The method according to any of the preceding claims, wherein at least one sequence polymorphism is assessed in a region corresponding to SEQ ID NO: 1 position 7760-22885 (RAI).

10 19. The method according to any of the preceding claims, wherein at least one sequence polymorphism is assessed in a region corresponding to SEQ ID NO: 1 position 34391- 37752.

15 20. The method according to any of the preceding claims, wherein at least two different probes are used, one probe being selected from the probes as defined in any of claims 13-16, and the other probe being capable of hybridising to a sequence different from SEQ ID NO: 1, or a part thereof, or to a sequence complementary to a region different from SEQ ID NO: 1, or a part thereof,.

20 21. The method according to claim 1, wherein the translational product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof, is an antibody, such as a monoclonal or polyclonal antibody.

25 22. A method for estimating the disease prognosis of an individual comprising
- assessing in the genetic material of a sample from said individual a sequence polymorphism

30 - in a region corresponding to SEQ ID NO: 2, or a part thereof, or
- in a region complementary to SEQ ID NO: 2, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 2, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 2, or a part thereof,
35 - obtaining a sequence polymorphism response,

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- estimating the disease prognosis of said individual based on the sequence polymorphism response.

5 23. The method according to claim 22, wherein the method has any of the features as defined in any of the claims 2-21.

10 24. A method for estimating a treatment response of an individual suffering from cancer to a disease treatment, comprising

- assessing in the genetic material of a sample from said individual a sequence polymorphism

15 - in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- in a region complementary to SEQ ID NO: 1, or a part thereof, or
- in a transcription product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof, or
- or translation product from a sequence in a region corresponding to SEQ ID NO: 1, or a part thereof,

20 - obtaining a sequence polymorphism response,

- estimating the individual's response to the disease treatment based on the sequence polymorphism response.

25 25. The method according to claim 24, wherein the method has any of the features as defined in any of the claims 2-21.

30 26. A primer or probe for detecting polymorphisms for use in a method as defined in any of the claims above, said primer or probe being selected from

35 TGGCTAACACGGTGAAACC (SEQ ID NO:7)
GGAATCCAAAGATTCTATGATGG (SEQ ID NO:8)
GGGAGGCGGAGCTTGACAGTGA (SEQ ID NO:9)
CTGAGATCGCACCACTGCAC (SEQ ID NO:10)
GGTTTCTGCTCTGCACACG (SEQ ID NO:11)

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CCTTTCTCCTTCCACCAACG (SEQ ID NO:12)
CGGGCTACAGGGTTACCTGAG (SEQ ID NO:13)
TCTGCAACCTGGTGCGAGCAGC (SEQ ID NO:14)
CCTACCACCATCATCACATCC (SEQ ID NO:15)
5 GCCTTGCCAAAAATCATAAC (SEQ ID NO:16)
CCTCTCCCAATTAAGTGCCTTCACACAGC (SEQ ID NO:17)
AGCCAGGGAGGTTGAGGCT (SEQ ID NO:18)
AGACAGCCCTGAATCAGCAC (SEQ ID NO:19)
GCAATGAGCCGAGATAGAA (SEQ ID NO:20)
10 TGGCTAGCCCACTACTCTA (SEQ ID NO:21)

27. The primer or probe according to claim 26, wherein the probe is operably linked to at least one label, such as operably linked to two different labels.

15 28. The probe according to claim 27, wherein the label is selected from TEX, TET, TAM, ROX, R6G, ORG, HEX, FLU, FAM, DABSYL, Cy7, Cy5, Cy3, BOFL, BOF, BO-X, BO-TRX, BO-TMR, JOE, 6JOE, VIC, 6FAM, LCRed640, LCRed705, TAMRA, Biotin, Digoxigenin, DuO-family, Daq-family.

20 29. The primer or probe according to any of claims 26-28, wherein the primer or probe is operably linked to a surface.

30. The primer or probe according to claim 29, wherein the surface is the surface of microbeads or a DNA chip.

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31. A kit for use in a method as defined in any of the claims above, comprising at least one primer or probe, said probe being as defined in any of claims 26-30, and optionally further amplifying means for nucleic acid amplification.

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